

Amendments to the Specification:

Please amend the specification as follows.

A. Updated Sequence Listing

Applicants have included herewith the following:

- 1) a CRF of an updated Sequence Listing;
- 2) a paper copy of the updated Sequence Listing;
- 3) a statement affirming that the paper copy and the CRF are identical and that the Sequence Listing adds no new matter;
- 4) a request that the updated Sequence Listing be entered into the specification:

Applicants respectfully request that the Sequence Listing provided herewith be entered into the specification and replace all prior versions of the Sequence Listing.

B. Paragraph [0011] of U.S. Publication 10/799,782

Please replace paragraph [0011] of U.S. Publication 10/799,782, which corresponds to the paragraph on page 4, lines 9-14 of the specification as filed on March 15, 2004, with the following rewritten paragraph:

[0011] FIG. 1. Comparison of the Flk-1 amino acid sequence with related RTKs. Amino acid sequence comparison of Flk-1 (SEQ ID NO: 9) with human KDR (SEQ ID NO: 10) and rat TKr-C (SEQ ID NO: 11). A section of the sequence which is known for all three receptors is compared and only differences to the Flk-1 sequence are shown.

C. Paragraph [0023] of U.S. Publication 10/799,782

Please replace paragraph [0023] of U.S. Publication 10/799,782, which corresponds to the paragraph on page 8, lines 1-2 of the specification as filed on March 15, 2004, and as amended in a reply filed April 9, 2008, with the following rewritten paragraph:

[0023] FIGS. 11-1, 11-2, 11-3 and 11-4. Nucleotide sequence (SEQ ID NO: 7) [~~SEQ ID NO: 1~~] and amino acid sequence (SEQ ID NO: 8) of murine [~~SEQ ID NO: 2~~] Flk-1.

D. Paragraph [0034] of U.S. Publication 10/799,782

Please replace paragraph [0034] of U.S. Publication 10/799,782, which corresponds to the paragraph on page 11, lines 18-28 of the specification as filed on March 15, 2004, with the following rewritten paragraph:

[0034] As explained in the working examples, infra, the polymerase chain reaction (PCR) method was used to isolate new receptor tyrosine kinases specifically expressed in post-implantation embryos and endothelial cells. One such clone was found to encode a RTK that had almost identical sequence homology with the previously identified cDNA clone isolated from populations of cells enriched for hematopoietic cells and designated fetal liver kinase-1 (Flk-1) (Matthews et al., 1991, Proc. Natl. Acad. Sci. U.S.A. 88: 9026-9030) (FIGS. 11-1 through 11-4) (~~FIGS. 11A and 11B~~).

E. Paragraph [0037] of U.S. Publication 10/799,782

Please replace paragraph [0037] of U.S. Publication 10/799,782, which corresponds to the paragraph on page 12, lines 10-13 of the specification as filed on March 15, 2004, with the following rewritten paragraph:

[0037] The nucleotide coding sequence and deduced amino acid sequence of the murine Flk-1 gene is depicted in FIGS. 11-1 through 11-4 11A and 11B (~~SEQ. ID NO. 1~~) (SEQ ID NOs: 7 and

8) and has recently been described in Matthews et al., 1991, Proc. Natl. Acad. Sci. U.S.A., 88: 9026-9030. In accordance with the invention, the nucleotide sequence of the Flk-1 protein or its functional equivalent in mammals, including humans, can be used to generate recombinant molecules which direct the expression of Flk-1; hereinafter, this receptor will be referred to as "Flk-1", regardless of the species from which it is derived.

F. Paragraph [0187] of U.S. Publication 10/799,782

Please replace paragraph [0187] of U.S. Publication 10/799,782, which corresponds to the paragraph on page 64 lines 31-36 continuing to page 65 lines 1-29 of the specification as filed on March 15, 2004, with the following rewritten paragraph:

[0187] To identify RTKs that are expressed during mouse development, PCR assays using two degenerate oligonucleotide primer pools that were designed on the basis of highly conserved sequences within the kinase domain of RTKs were performed (Hanks, S. K. et al. 1988, Science 241: 42-52). DNA extracted from a λgt10 cDNA library of day 8.5 mouse embryos (Fahrner, K. et al., 1987, EMBO J., 6: 1497-1508), a stage in mouse development at which many differentiation processes begin was used as the template in the PCR assays. In a parallel approach, with the intention of identifying RTKs that regulate angiogenesis, similar primers were used for the amplification of RTK cDNA sequences from capillary endothelial cells that had been isolated from the brains of postnatal day 4-8 mice, a time at which brain endothelial cell proliferation is maximal (Robertson, P. L. et al., 1985, Devel. Brain Res. 23: 219-223). Both approaches yielded cDNA sequences (FIG. 11, SEQ. ID NO. 7 [:]) encoding the recently described fetal liver RTK, Flk-1 (Matthews, W. et al., 1991, Proc. Natl. Acad. Sci. U.S.A. 88: 9026-9030). Based on amino acid homology, this receptor is a member of the type III subclass of RTKs (Ullrich, A. and Schlessinger, J. 1990, Cell 61: 203-212) and is closely related to human fit, which also contains seven immunoglobulin-like repeats in its extracellular domain in contrast to other RTKs of that subfamily, which contain only five such repeat structures (Matthews, W. et al., 1991, Proc. Natl. Acad. Sci. U.S.A. 88: 9026-9030). Sequence comparisons of Flk-1 with

KDR (Terman, B. I. et al., 1991, Oncogene 6: 1677-1683) and TKr-C (Sarzani, R. et al., 1992, Biochem. Biophys. Res. Comm. 186: 706-714) suggest that these are the human and rat homologues of Flk-1, respectively (FIG. 1).